



UNITED STATES PATENT AND TRADEMARK OFFICE

UNITED STATES DEPARTMENT OF COMMERCE
United States Patent and Trademark Office
Address: COMMISSIONER FOR PATENTS
P.O. Box 1450
Alexandria, Virginia 22313-1450
www.uspto.gov

APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/519,173	04/19/2005	Glenn D. Prestwich	21101.0036U2	5246
23859	7590	10/31/2006	EXAMINER	
NEEDLE & ROSENBERG, P.C. SUITE 1000 999 PEACHTREE STREET ATLANTA, GA 30309-3915			LUKTON, DAVID	
			ART UNIT	PAPER NUMBER
			1654	

DATE MAILED: 10/31/2006

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary

Application No.

10/519,173

Applicant(s)

PRESTWICH ET AL.

Examiner

David Lukton

Art Unit

1654

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

- 1) ☒ Responsive to communication(s) filed on 15 June 2006.
- 2a) ☐ This action is **FINAL**. 2b) ☒ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

- 4) ☒ Claim(s) 1-115 is/are pending in the application.
- 4a) Of the above claim(s) 4-6, 10-12 and 15-115 is/are withdrawn from consideration.
- 5) ☐ Claim(s) _____ is/are allowed.
- 6) ☒ Claim(s) 1-3 and 13 is/are rejected.
- 7) ☒ Claim(s) 7-9 and 14 is/are objected to.
- 8) ☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on _____ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

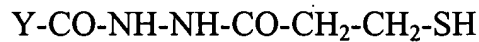
Priority under 35 U.S.C. § 119

- 12) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☐ All b) ☐ Some * c) ☐ None of:
1. ☐ Certified copies of the priority documents have been received.
2. ☐ Certified copies of the priority documents have been received in Application No. _____.
3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).
- * See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

- 1) ☒ Notice of References Cited (PTO-892)
- 2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
- 3) ☒ Information Disclosure Statement(s) (PTO/SB/08)
Paper No(s)/Mail Date _____
- 4) ☐ Interview Summary (PTO-413)
Paper No(s)/Mail Date. _____
- 5) ☐ Notice of Informal Patent Application
- 6) ☐ Other: _____

Applicant's election of Group 1 (claims 1-14, 41-49) without traverse is acknowledged, as is the elected specie, which is the following ("Y" is gelatin):



Claims 4-6, 10-12, 41-49 are withdrawn from consideration, as they do not encompass the elected specie.

Claims 1-3, 7-9, 13, 14 are examined in this Office action; claims 4-6, 10-12, 15-115 are withdrawn from consideration.

In this Office action, claims 1-3 and 13 are rejected, and claims 7-9 and 14 are objected to because of their dependence on rejected claims.



The following is a quotation of 35 USC, §103 which forms the basis for all obviousness rejections set forth in the Office action:

A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negated by the manner in which the invention was made.

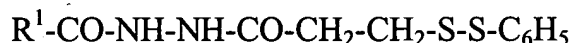
Subject matter developed by another person, which qualifies as prior art only under subsection (f) and (g) of section 102 of this title, shall not preclude patentability under this section where the subject matter and the claimed invention were, at the time the invention was made, owned by the same person or subject to an obligation of assignment to the same person.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103, the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made, absent any evidence to the contrary. Applicant is advised of the obligation under 37 C.F.R. 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later

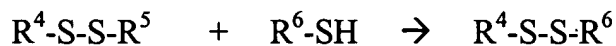
invention was made in order for the examiner to consider the applicability of potential 35 U.S.C. 102(f) or (g) prior art under 35 U.S.C. 103.

Claims 1-3 and 13 are rejected under 35 U.S.C. §103 as being unpatentable over Thorpe (USP 5,762,918).

Thorpe discloses (col 26, line 29+) the following, wherein R¹ represents heparin, R² is pyridine and R³ is the "A" chain of ricin:



In instant claim 1, variable "Q" can be a sulfhydryl group. But "Q" can also be a "thiol-reactive electrophilic functional group". As it happens, disulfide bonds meet this latter limitation. As applicants are no doubt aware, compounds containing disulfide bonds are far from inert, and will undergo disulfide exchange as follows (R⁴, R⁵ and R⁶ arbitrarily selected):



[The equilibrium position will depend primarily on the stoichiometry of the reactants and pH of the medium]. Thus, in the compounds disclosed by Thorpe, one of the sulfur atoms (of the disulfide moiety) qualifies as a "thiol-reactive electrophilic

functional group”; there is no requirement that the “electrophilic group” in question be a carbon atom.

Thus, the claims are rendered obvious.



Claim 1 is rejected under 35 U.S.C. §103 as being unpatentable over Janda (USP 6664372).

Janda discloses (col 4, lines 51-57) a compound which contains the requisite dicarbonyl hydrazine group. At one terminus of the compound there is a variable “Rx”; it is recited at col 4, line 62 that this Rx group can be the side chain of cysteine.

Thus, the claims are rendered obvious.

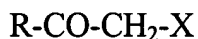


Claims 1-3 and 13 are rejected under 35 U.S.C. §103 as being unpatentable over Pouyani (USP 5,616,568).

Pouyani discloses structure 2e in column 12. This compound falls within the scope of claim 1 because, as noted above, a disulfide bond qualifies as a “thiol-reactive electrophilic functional group”. At the same time, the exclusion of hyaluronan only applies if “Q” is a thiol group (*per se*). The claims are rendered obvious on this basis.

Separate from the foregoing, there is a hydrocortisone/hemisuccinate/hyaluronate conjugate provided in the space spanning cols 21-22 (approx line 15+). As it

happens, there are three separate sites that would qualify as a "thiol-reactive electrophilic functional group". First is the ester bond; this will react with, e.g., butanethiol to form a thioester. Second, is the position which is alpha to the exocyclic keto group of the hydrocortisone; as applicants are aware, the methylene group is particularly electrophilic in compounds which conform to the following (R = alkyl, and X = leaving group):



In the Pouyani compound, the leaving group would be a carboxylate anion.

In addition to the foregoing, there is the enone present in the hydrocortisone molecule which will react with thiols; the issue of Michael addition of thiols is discussed, e.g., in the Lutolf reference of record (*Bioconjugate Chem* 12, 1051, 2001).

Thus, for several reasons, the claims are rendered obvious.



- Applicants are requested to note that there is a spelling error in claim 6 ("polyaspratic").
- Reference A159 was stricken from the IDS. The date of publication should be provided.

No claim is allowed.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to David Lukton whose telephone number is 571-272-0952. The examiner can normally be reached Monday-Friday from 9:30 to 6:00.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Cecilia Tsang, can be reached at (571)272-0562. The fax number for the organization where this application or proceeding is assigned is 571-273-8300.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is 571-272-1600.

A handwritten signature in cursive script, appearing to read "D. Lukton".

DAVID LUKTON, PH.D.
PRIMARY EXAMINER